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Extended Heterocyclic Systems 2.[1] The Synthesis and Characterisation of (2-Furyl)pyridines , (2-Thienyl)pyridines, and Furan-Pyridine and Thiophene-Pyridine Oligomers

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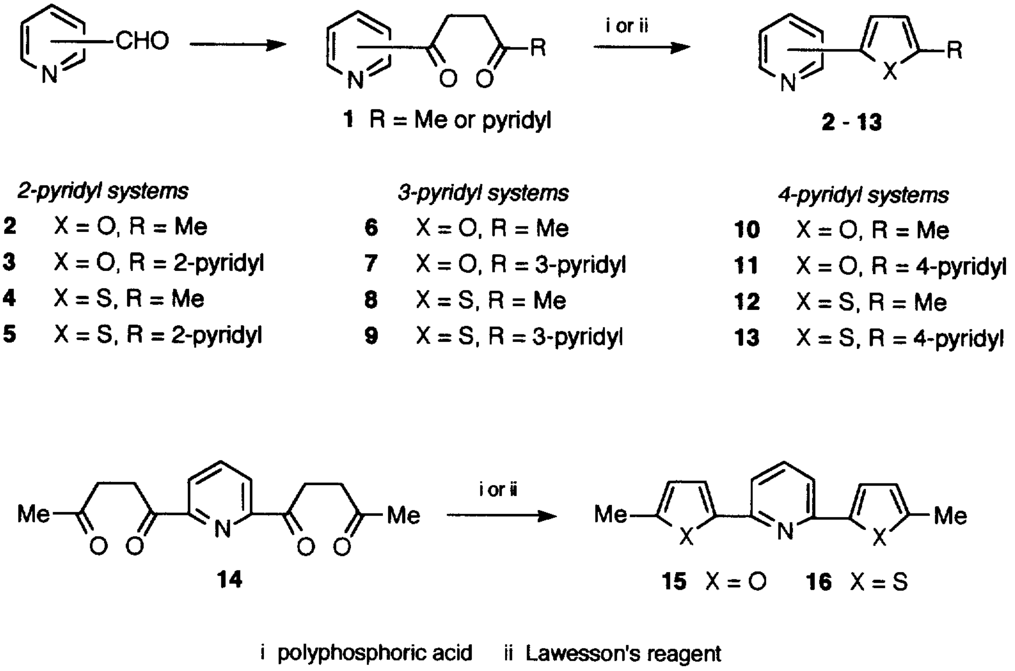
***Abstract*:** The Stetter procedure has been adapted to produce simple 2-furyl- and 2-thienyl-pyridines and their related oligomers, which have been characterised by ^{13}C NMR spectroscopy. σ values for the 2-furyl and 2-thienyl rings have been deduced from the pK_a values of the conjugate acids of the 2-furyl- and 2-thienylpyridines. © 1997 Elsevier Science Ltd.

Following our recent report[1] describing the synthesis of oligomeric and polymeric alternating pyrrole:pyridine systems, we now report the synthesis and characterisation of the corresponding oligomeric furan:pyridine and thiophene:pyridine systems.

Prior to the commencement of our work, of the relatively few methods described for the synthesis of thienylpyridines[2] many involved the reaction of thienyl Grignard reagents or lithiothiophenes[3-5] with halogenopyridines and the yields were generally poor (2 - 35%). Higher yields (60 - 80%) have been attained using palladium or nickel catalysed coupling reactions[6] and heteroarylboron derivatives.[7,8] Photochemical[9] and Gomberg-type[10] coupling reactions have also been reported. However, although the higher yielding procedures are acceptable for the synthesis of simple thienylpyridines, they are not readily extended to the synthesis of oligomeric thiophene:pyridine systems. Photochemical[9] and Gomberg-type[10,11] and borane-mediated[8] coupling reactions have also been utilised for the synthesis of furylpyridines. Isomeric (2-furyl)pyridines have also been obtained in good yield *via* a Hansch-type reaction from pyridinoylacetates.[12]

Utilising procedures analogous to those described in our earlier paper,[1] we have now obtained furylpyridines and thienylpyridines from formylpyridines, *via* the Paal reaction on the intermediary pyridyl-1,4-diketones[1,13] **1** using polyphosphoric acid or Lawesson's reagent[14], respectively (Scheme 1). The ketonic precursor **14** for the 2,6-bis(2-furyl)- and 2,6-bis(2-thienyl)pyridines, **15** and **16** , was readily obtained by the Stetter reaction on 2,6-diformylpyridine.

As with the corresponding pyrrole:pyridine systems, the simple furyl and thienylpyridines were best characterised by their ^{13}C NMR spectra (Table 1) and the data could be used in the analysis of the polymeric systems. In general, the chemical shifts for the substituted pyridine rings, relative to the unsubstituted ring, suggest that the mesomeric effect of the five-membered rings contributes less to the interaction between the two rings than does their inductive effects. Significantly, it would appear that the thiophene ring is more electron-withdrawing in its overall electronic effect than is the furan ring (see also the pK_a data, Tables 2 and 3).



2-pyridyl systems
2 X = O, R = Me
3 X = O, R = 2-pyridyl
4 X = S, R = Me
5 X = S, R = 2-pyridyl

3-pyridyl systems
6 X = O, R = Me
7 X = O, R = 3-pyridyl
8 X = S, R = Me
9 X = S, R = 3-pyridyl

4-pyridyl systems
10 X = O, R = Me
11 X = O, R = 4-pyridyl
12 X = S, R = Me
13 X = S, R = 4-pyridyl

i polyphosphoric acid ii Lawesson's reagent

Scheme 1

Table 1 Mean ^{13}C NMR Chemical Shifts for the Pyridine Rings of 2-, 3- and 4-(2-Furyl and Thienyl)pyridines and Related Pyrrolylpyridines[1]

	2-C	3-C	4-C	5-C	6-C
2-Substituted Pyridines					
2-Furyl	**153.7±0.3**	121.7±0.4	136.5±0.1	116.9±0.4	150.8±0.8
2-Thienyl	**151.8±0.8**	127.6±0.1	137.6±0.8	124.0±0.5	149.0±0.5
2-Pyrrolyl	**150.7±0.7**	120.5±0.7	136.4±0.5	118.7±0.5	149.5±0.2
3-Substituted Pyridines					
2-Furyl	152.1±0.8	**126.7±0.4**	130.3±0.3	123.4±0.1	148.8±0.4
2-Thienyl	148.1±0.3	**130.3±0.4**	132.6±0.2	126.0±0.5	146.4±0.1
2-Pyrrolyl	147.5±1.1	**130.0±0.7**	132.1±1.8	123.5±0.3	146.0±1.0
4-Substituted Pyridines					
2-Furyl	152.9±1.0	117.4±0.2	**136.8±0.8**	117.4±0.2	152.9±1.0
2-Thienyl	150.3±0.1	119.5±0.1	**139.6±0.9**	119.5±0.1	150.3±0.1
2-Pyrrolyl	149.8±0.1	117.7±0.6	**139.0±0.4**	117.7±0.6	149.8±0.1

The greatest enhancement of electron density on the substituted pyridine rings, as correlated with the largest upfield shift of the ^{13}C NMR signals (Figure 1), generally occurs "ortho" to the position of substitution by the 2-heteroaryl group and, somewhat surprisingly, is particularly significant for the 2-furyl derivatives. Also, in the case of the 2-(2-heteroaryl)pyridines, large upfield shifts are also noted at the 5-position (i.e. "para" to the heteroaryl substituent). The downfield shifts of the ^{13}C NMR signals for the carbon atoms at the point of substitution on the pyridine ring are consistent with significant inductive electron-withdrawing effects of the 2-heteroaryl rings. These observations are similar to those alluded to by Kauffmann.[2]

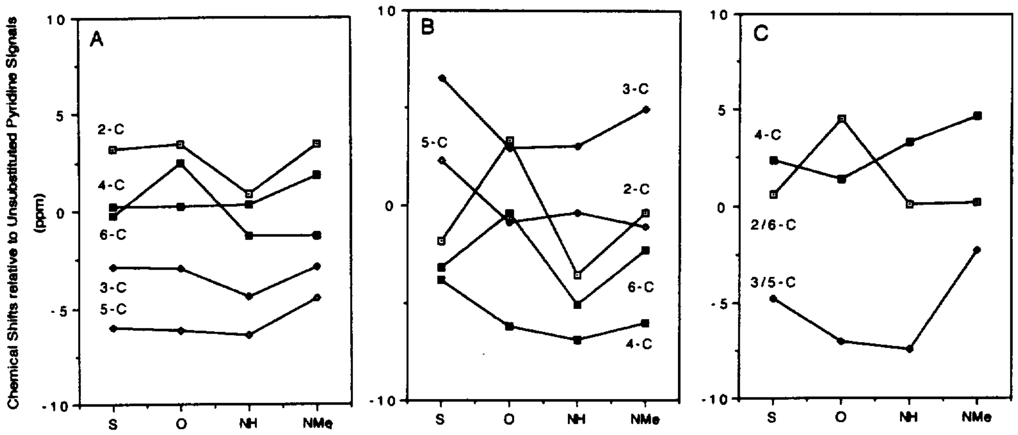


Figure 1. ^{13}C NMR chemical shifts for the pyridine rings of **2**, **4** and related 2-(2-pyrrolyl and 1-methyl-2-pyrrolyl)pyridines (A); **6**, **8** and related 3-(2-pyrrolyl and 1-methyl-2-pyrrolyl)pyridines (B); and **10**, **12** and related 4-(2-pyrrolyl and 1-methyl-2-pyrrolyl)pyridines (C), relative to unsubstituted pyridine

The simple furyl- and thienylpyridines are weaker bases than the corresponding pyrrolylpyridines (Tables 2 and 3) and, with the exception of the 4-substituted isomers, they are also weaker bases than pyridine indicating a significant electron-withdrawing inductive effect of both the 2-furyl and 2-thienyl rings. It is noteworthy that the thienyl systems are consistently less basic than the corresponding furan derivatives. Comparison of the pKa values with those of other substituted pyridines allows a correlation to be made with the Hammett σ values. Using σ_{meta} values, a good correlation (0.970) was obtained for the pK_a values of the 3-substituted pyridines, which gave σ_{meta} values of 0.10 and 0.95 for the 2-thienyl and 2-furyl systems, respectively, compared with -0.27 calculated for the 2-pyrrolyl system. A good correlation ($r = 0.970$) of σ_{para} with the pKa values of 4-substituted pyridines gave σ_{para} values of -0.08 for both the 2- furyl and 2-thienyl systems, compared with -0.48 for the 2-pyrrolyl system. A slightly less good correlation ($r = 0.943$) with $\sigma+$ for the 4-substituted pyridines gave values of -0.32, -0.22 and -0.94 for the 2-furyl, 2-thienyl and 2-pyrrolyl systems, respectively. These results fall within the wide range of σ values, determined using different criteria, that have been recorded for the thienyl and furyl systems.[15]

Table 2. pK_a Values of the Conjugate Acids of Furyl- and Thienylpyridines (**2**, **4**, **6**, **8**, **10**), 2,6-Bis(5-methylfur-2-yl)- and 2,6-Bis(5-methylthien-2-yl)pyridines (**15** and **16**), and Related (5-Methylpyrrol-2-yl)pyridines[a]

	5-Methylfur-2-yl Derivatives (**2**, **6**, **10**, **15**)	5-Methylthien-2-yl Derivatives (**4**, **8**, **12**, **16**)	5-Methylpyrrol-2-yl Derivatives
2-Substituted Pyridines	4.24±0.005[b] (4.18±0.5)[c]	3.99±0.006[b] (3.79±0.012)[d]	5.87±0.01[b] (5.20 - 5.35)[b,e]
3-Substituted Pyridines	4.67±0.004[b,f] (4.59±0.1; 4.62±0.06)[c]	4.56±0.003[b] (4.51±0.006)[d]	5.42±0.01[b]
4-Substituted Pyridines	5.70±0.005[b] (5.60±0.08)[c]	5.68±0.004[b] (5.59±0.003)[d]	7.83±0.05[b]
2,6-Disubstituted Pyridines	3.24±0.006[g]	2.68±0.003[b]	

[a] Taken from refs. 1, 16 and 17. [b] determined spectroscopically. [c] data for 2-furyl derivatives.[11b, 12b] [d] data for 2-thienyl derivatives.[3b] [e] data for 1-alkyl-5-methylpyrrol-2-yl derivatives. [f] *cf.* lit.[11b] value of 4.63±0.015 [g] determined potentiometrically.

Table 3. pK_a Values of the Conjugate Acids of 2,5-Bis(2-, 3- and 4-Pyridyl)furans (**3**, **7**, **11**) and 2,5-Bis(2-, 3- and 4-Pyridyl)thiophenes (**5**, **9**, **13**).[a]

	2,5-Disubstituted Furan Derivatives (**3**, **7**, **11**)	2,5-Disubstituted Thiophene Derivatives (**5**, **9**, **13**)
2-Pyridyl Compounds	pK_a1 3.41±0.060 pK_a2 3.20±0.040	pK_a1 2.92±0.010 pK_a2 2.59±0.070
3-Pyridyl Compounds	pK_a1 3.66±0.007 pK_a2 2.32±0.010	pK_a1 3.50±0.015 pK_a2 3.06±0.006
4-Pyridyl Compounds	pK_a1 4.51±0.006 pK_a2 2.39±0.015	pK_a1 4.49±0.015 pK_a2 2.98±0.005

[a] determined potentiometrically

Semi-empirical AM1 calculations[18] on the preferred conformations of the heterocyclic rings of compounds **2**, **6** and **10**, **4**, **8** and **12**, and their pyrrolyl analogues are presented in Table 4, together with the calculated inter-ring bond lengths and bond orders. The calculated conformations can be rationalised in terms of the interactions between the dipole moments of the heterocyclic rings and steric hindrance between substituents on the pyrrolyl nitrogen atom and the pyridine system. The inter-ring bond lengths suggest that the mesomeric interaction between the rings is not great and is compatible with the deductions made on the basis of the pK_a values.

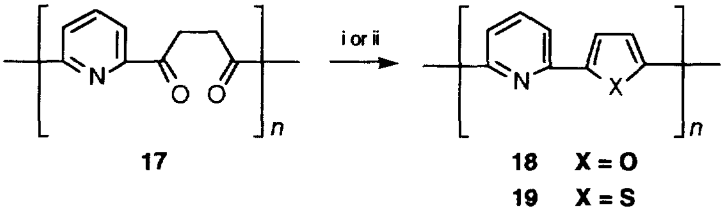
Although the 2-(5-methylfur-2-yl)- and 2-(5-methylthien-2-yl)pyridines are 40 to 80 times less basic respectively than 2-(5-methylpyrrol-2-yl)pyridine, they were more readily N-alkylated than the pyrrole system under "standard" conditions in refluxing ethanol to give the pyridinium salts. This observation has been rationalised in terms of intramolecular H-bonding within the 2-(5-methylpyrrol-2-yl)pyridine reducing the nucleophilicity of the pyridine nitrogen atom,[1,17] as the non-H-bonded 2-(1-alkyl-5-methylpyrrol-2-yl)pyridines have reactivities comparable with those of the 2-thienyl and 2-furyl systems, and the 3- and 4-(5-methylpyrrol-2-yl)pyridines were more readily N-alkylated than are the corresponding 3- and 4-furyl and thienylpyridines.[17] Although there is a significant difference in the first and second pK_a values of the conjugate acids of the 2,5-bis(3- and 4-pyridyl)furans and thiophenes, they gave only the di-N-methylpyridinium salts under the "standard" conditions without isolation of the mono-N-methylated derivatives. In contrast, N-methylation of 2,5-bis(2-pyridyl)furan and thiophene, where the first and second pK_a values differ by *ca.* 0.5, under "standard" conditions yielded only the mono-N-methylated derivatives and more vigorous conditions (100°C in a sealed vessel) for an extended reaction time (2 weeks) was required to produce the di-N-methylated salts. Even under the most vigorous of reaction conditions, the 2,6-bis(2-heteroaryl)pyridines, **15** and **16**, failed to produce the N-methylpyridinium salts, presumably owing to the additional steric hindrance of the second heteroaryl groups.

Table 4. Calculated Inter-ring Conformations and Inter-ring C-C Bond Distances and π-Bond Orders.[a]

Compound	Dihedral Angle (°)	Bond Angle (°)	Bond Angle (°)	Bond Lengths (Å)	π-Bond Order
2-Pyridyl Systems	N^{1}-C^{2}-$C^{2'}$-$X^{1'}$	N^{1}-C^{2}-$C^{2'}$	C^{2}-$C^{2'}$-X	C^{2}-$C^{2'}$	C^{2}-$C^{2'}$
5-Methyl-fur-2-yl (**2**)	180±2	117.7	116.9	1.452	0.18
5-Methylthien-2-yl (**4**)	0±6	117.9	122.8	1.452	0.18
5-Methylpyrrol-2-yl	0±2	119.2	123.8	1.459	0.16
1,5-Dimethylpyrrol-2-yl	21±1	120.1	126.0	1.460	0.15
1-Ethyl-5-methylpyrrol-2-yl	33±1	120.7	127.4	1.460	0.15
3-Pyridyl Systems	C^{2}-C^{3}-$C^{2'}$-$X^{1'}$	C^{2}-C^{3}-$C^{2'}$	C^{3}-$C^{2'}$-$X^{1'}$	C^{3}-$C^{2'}$	C^{3}-$C^{2'}$
5-Methylfur-2-yl (**6**)	180±1	120.1	117.2	1.437	0.22
5-Methylthien-2-yl (**8**)	23±2	120.7	122.8	1.438	0.22
5-Methylpyrrol-2-yl	22±2	120.2	124.4	1.460	0.15
1,5-Dimethylpyrrol-2-yl	40±1	122.2	125.3	1.448	0.19
1-Ethyl-5-methylpyrrol-2-yl	46.5±1	122.1	125.7	1.448	0.19
4-Pyridyl Systems	C^{3}-C^{4}-$C^{2'}$-$X^{1'}$	C^{3}-C^{4}-$C^{2'}$	C^{4}-$C^{2'}$-$X^{1'}$	C^{4}-$C^{2'}$	C^{4}-$C^{2'}$
5-Methyl-2-furyl (**10**)	0±1	121.7	117.4	1.440	0.21
5-Methylthien-2-yl (**12**)	20±2	120.8	122.9	1.441	0.21
5-Methylpyrrol-2-yl	19±3	122.5	124.2	1.447	0.19
1,5-Dimethylpyrrol-2-yl	38±2	122.6	125.6	1.449	0.19
1-Ethyl-5-methylpyrrol-2-yl	45±1	122.5	125.9	1.450	0.19

[a] estimated error ± 0.04

The conversion of the polymeric 1-(2-pyridyl)butan-1,4-dione **17**, derived from the bis-Mannich base of 2,6-diacetylpyridine and 2,6-diformylpyridine,[1] into the alternating polymeric furan:pyridine and thiophene:pyridine systems, **18** and **19**, was not as effective as the analogous successful formation of the pyrrole:pyridine polymer.[1] The absence of νC=O absorption in the infrared spectra of the reaction products and the absence of ^{13}C NMR spectral evidence for the butan--1,4-dione system suggested the complete reaction of the ketonic polymer, while the presence of the appropriate aromatic ^{13}C NMR signals (Table 4) indicated the partial formation of the five-membered heterocyclic rings. However, elemental analytical data showed that the Paal reaction was incomplete and that phosphorus-containing residues were retained in the polymers. All attempts to obtain analytically pure sample failed. Molecular modelling experiments indicate that the heterocyclic polymers adopt a helical structure with four repeating units in each cycle, which could restrict the elimination of the phosphorus-containing substrates in the final stages of the ring formation.



i polyphosphoric acid ii Lawesson's reagent

EXPERIMENTAL

Infrared spectra were recorded for mulls in Nujol or as liquid films using a Perkin-Elmer 295 spectrometer and the ^{1}H NMR spectra at 60 or 90 MHz were measured for *ca.* 25 - 30% solutions in $CDCl_3$, unless otherwise indicated, using a JEOL EX-90Q or JEOL GX-400 spectrometer. ^{13}C NMR spectra were measured using the JEOL EX-90Q and JEOL GX-400 spectrometers at 22.5 and 100 MHz, respectively. All chemical shifts are expressed relative to Me_4Si. Solid state ^{13}C NMR spectra of the polymeric materials were obtained at 50.29 MHz using the UEA 200 spectrometer. Electronic spectra were measured for *ca.* 10^{-5} solutions in ethanol using a Pye-Unicam SP200 spectrometer. pKa values were determined spectroscopically or potentiometric methods using standard procedures.[19]

1-(2-, 3- and 4-Pyridyl)butan-1,4-diones:

With the exception of compound **14**, All pyridylbutan-1,4-diones were prepared by the Stetter procedure and had m.p.'s and spectroscopic properties identical to those described in the literature.[1]

2,6-Di(1,4-dioxopent-1-yl)pyridine **14**: But-3-en-2-one (3.5 g, 50 mmol), 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride (1.62 g, 6 mmol) and dry triethylamine (3.03 g, 3 mmol) in dry dioxane (10 ml) were heated at 90 - 100°C under nitrogen. 2,6-Diformylpyridine (2.7 g, 20 mmol) in dry dioxane (20 ml) was added dropwise slowly over a period of 2 h, and the mixture was then stirred at 90-100°C for further

12h. The mixture was cooled to room temperature and the solvents were removed under vacuum. Water (300 ml) was added and the aqueous layer was extracted with dichloromethane (3 x 50 ml). The combined organic extracts were washed brine (2 x 10 ml) and dried ($MgSO_4$). Removal of the solvent gave a crude product, which was purified by chromatography from silica gel, using ethyl acetate:petroleum ether (1:1) as the eluant, and recrystallisation from ethanol to give *2,6-di(1,4-dioxopent-1-yl)pyridine* (4.18 g, 76%), m.p. 93 - 94°C (Found: C, 65.3; H, 5.1; N, 5.1 $C_{15}H_{17}NO_4$ requires C, 65.5; H, 6.2; N, 5.1%). δ_H 2.26 (6H, s), 2.92 (4H, t), 3.57 (4H, t), 7.95 - 8.23 (3H, m); δ_C .22.9 (q), 31.7 (t), 37.0 (t), 124.8 (d), 138.0 (d), 152.2 (s), 199.5 (s), 206.9 (s).

General procedure for the conversion of the 1,4-dicarbonyl compounds into furans:

The appropriate diketone (8 mmol) and polyphosphoric acid (10.0 - 12.0 g) were stirred and heated for 4 - 6h at 130 - 170°C. The reaction mixture was poured into the crushed ice (100 g), neutralised with aqueous. Na_2CO_3, and extracted dichloromethane (2 x 100 ml). The extracts were dried ($MgSO_4$) and evaporated to yield the crude furans, which were further purified either by recrystallisation from dichloromethane:hexane or ethanol:diethyl ether or, in the cases of liquids, by distillation.

1-(2-Pyridyl)pentan-1,4-dione gave *2-(5-methylfur-2-yl)pyridine* **2** (82%), b.p. 104 - 105°C at 7 mm Hg (lit.,[21] 120°C at 14 mm Hg) (Found: C, 75.3; H, 5.8; N, 8.8 Calc. for $C_{10}H_9NO$: C, 75.5; H, 5.7; N, 8.8%). δ_H 2.36 (3H, s), 6.09 (1H, d), 7.01 (2H, m), 7.58 (2H, dd), 8.58 (1H, dd); δ_C 13.7 (q), 108.3 (d), 109.8 (d), 118.0 (d), 121.2 (d), 136.4 (d), 149.5 (s), 149.6 (s), 152.1 (d), 153.4 (s).

1-(3-Pyridyl)pentan-1,4-dione gave *3-(5-methylfur-2-yl)pyridine* **6** (83%), b.p. 122 - 125°C at 10 mm Hg (lit.,[26] 72°C at 0.5 mm Hg) (Found: C, 75.4; H, 5.5; N, 8.9 Calc. for $C_{10}H_9NO$: C, 75.5; H, 5.7; N, 8.8%) δ_H 2.31 (3H, s), 6.01 (1H, d), 6.54 (1H, d), 7.18 (1H, m), 7.80 (1H, m), 8.39 (1H, dd), 8.95 (1H, d); δ_C 13.5 (q), 107.4 (d), 108.0 (d), 123.3 (d), 127.1 (s), 130.0 (d), 144.9 (s), 147.5 (s), 149.2 (d), 152.9 (d).

1-(4-Pyridyl)pentan-1,4-dione gave *4-(5-methylfur-2-yl)pyridine* **10** (81%), m.p. 63 - 65°C (Found: C, 75.4; H, 5.6; N, 8.8 $C_{10}H_9NO$ requires C, 75.5; H, 5.7; N, 8.8%). δ_H 2.34 (3H, s), 6.07 (1H, dd), 6.72 (1H, d), 7.42 (2H, dd), 8.53 (2H, dd); δ_C 13.7 (q), 108.4, (d) 109.8 (d), 117.2 (d), 137.6 (s), 149.6 (s), 150.1 (s), 154.1 (d).

2,6-Bis(5-methylfur-2-yl)pyridine **15** (74%) m.p. 128 - 130°C (Found: C, 75.0; H, 5.4; N, 5.7 $C_{15}H_{13}NO_2$ requires C, 75.3; H, 5.5; N, 5.9%). δ_H 2.48 (6H, s), 6.09 (2H, d), 7.01 (2H, d), 7.20 - 7.80 (3H, m); δ_C 13.8 (q), 108.2 (d), 109.9 (d), 115.7 (d), 136.9 (d), 149.2 (s), 152.2 (s), 153.3 (s).

2,5-Di(2-pyridyl)furan **3** (82%) m.p. 123 - 125°C (Found: C, 75.4; H, 4.6; N, 12.6 $C_{14}H_{10}N_2O$ requires C, 75.7; H, 4.5; N, 12.6%). δ_H 7.00 - 7.20 (4H, m), 7.50 7.90 (4H, m), 8.61 (2H, dd); δ_C 111.0 (d), 118.7 (d), 122.1 (d), 136.5 (d), 149.0 (s), 149.6 (d), 154.0 (s); *2,5-di(3-pyridyl)furan* **7** (92%) had m.p. 159 - 160°C; (Found: C, 75.4; H, 4.5; N, 12.6 $C_{14}H_{10}N_2O$ requires C, 75.7; H, 4.5; N, 12.6%). δ_H 6.83 (2H, dd), 7.32 (2H, dd), 7.97 (2H, dd), 8.52 (2H, dd), 8.97 (2H, s); δ_C 108.6 (d), 123.5, (d) 126.3, (s) 130.6 (d), 145.3 (s), 148.4 (d), 151.2 (d); *2,5-di(4-pyridyl)furan* **11** (55%) had m.p. 156.5 158°C (Found: C, 72.5; H, 5.0; N, 10.2 $C_{14}H_{10}N_2O$ 0.5H_2O requires C, 72.7; H, 4.8; N, 12.1 %). δ_H 7.48 (2H, s), 7.85 (2H, d), 8.65 (2H, d); δ_C 112.1 (d), 117.6 (d), 136.0 (s), 150.2 (s), 151.6 (d) were obtained from 2,5-di(2-pyridyl-, 3-pyridyl- and 4-pyridyl)butan-1,4-dione, respectively.

General procedure for the conversion of the 1,4-dicarbonyl compounds into thiophenes:

The appropriate diketone (8 mmol) and Lawesson's reagent (2.30 g, 5.5 mmol) in dry toluene (100 ml) were kept under nitrogen at 110°C for 50 h. When the reaction was complete, as indicated by TLC analysis, the mixture was allowed to cool to room temperature and the solvent removed. The crude product was purified by flash column chromatography from silica gel, using ethyl acetate:petroleum ether (1:1) as the eluant. Recrystallisation from ethanol or dichloromethane:diethyl ether gave the analytically pure thiophenes.

1-(2-Pyridyl)pentan-1,4-dione gave *2-(5-methylthien-2-yl)pyridine* **4** (69%), m.p. 78 - 79°C (Found: C, 68.3; H, 5.2; N, 7.9; S, 18.5 $C_{10}H_9NS$ requires C, 68.5; H, 5.2; N, 8.0; S, 18.5%). δ_H 2.52 (3H, s), 6.76 (1H, dd), 7.11 (1H, m), 7.36 (1H, d), 7.56 (2H, m), 8.50 (1H, dt); δ_C 15.6 (q), 118.2 (d), 121.3 (d), 124.6 (d), 127.5 (d), 136.4 (d), 142.3 (s), 142.4 (s), 149.4 (d), 152.8 (s) .

1-(3-Pyridyl)pentan-1,4-dione gave *3-(5-methylthien-2-yl)pyridine* **8** (64%), m.p. 67.5 - 69°C (Found: C, 68.3; H, 5.2; N, 7.9; S, 18.5 $C_{10}H_9NS$ requires C, 68.5; H, 5.2; N, 8.0; S, 18.5%). δ_H 2.48 (3H, s), 6.71(1H, dd), 7.17 (2H, m), 7.76 (1H, m), 8.41 (1H, dd), 8.78 (1H, d); δ_C 15.3 (q), 123.5 (d), 124.1 (d), 126.5, (d) 130.7 (s), 132.4 (d), 137.8 (s), 140.9 (s), 146.4 (d), 147.8 (d).

1-(4-Pyridyl)pentan-1,4-dione gave *4-(5-methylthien-2-yl)pyridine* **12** (51%), m.p. 139 - 140°C (Found: C, 68.4; H, 5.2; N, 7.9; S, 18.5 $C_{10}H_9NS$ requires C, 68.5; H, 5.2; N, 8.0; S, 18.5%). δ_H 2.53 (3H, s), 6.78 (1H, dd), 7.31 (1H, dd), 7.39 (2H, dd), 8.57 (2H, dd); δ_C 15.3 (q), 119.4 (d), 125.4 (d), 126.7 (d), 138.6 (s), 141.6 (s), 142.4 (s), 150.2 (d).

2,6-Bis(5-methylthien-2-yl)pyridine **16** (55%), m.p. 115 - 117°C (Found: C, 66.4; H, 4.9; N, 5.0; S, 23.7 $C_{15}H_{13}NS_2$ requires C, 66.4; H, 4.8; N, 5.2; S, 23.6%) was obtained from 2,6-(1,4-dioxopentyl)pyridine. δ_H 2.55 (6H, s), 6.74 (2H, dd), 7.39 (4H, m), 7.56 (1H, dd); δ_C 15.6 (q), 115.6 (d), 124.6 (d), 126.2 (d), 136.9 (d), 142.4 (s), 142.5 (s), 152.1 (s).

2,5-Di(2-pyridyl)thiophene **5** (46%) m.p. 161 - 162°C (lit., m.p.[3] 162 - 163°C). δ_H 7.00 - 7.34 (2H, m), 7.64 (6H, d), 8.56 (1H, dd); δ_C (DMSO-d_6) 119.9 (d), 123.3 (d), 127.6 (d), 138.8 (d), 145.1 (s), 148.6 (d), 150.7 (s); 2,5-Di(3-pyridyl)thiophene **9** (53%) m.p. 94 - 95.5°C (lit., m.p.[1,36] 97°C). δ_H 7.30 (m, 2H), 7.83 (dd, 2H), 8.48 (dd, 2H), 8.84 (d, 2H); δ_C 123.7 (d), 125.4 (d), 129.9 (s), 132.8 (d), 140.6 (s), 146.4 (d), 148.4 (d); *2,5-Di(4-pyridyl)thiophene* **13** (37%) m.p. 176.5 - 180°C (Found: C, 70.6; H, 4.1; N, 11.7; S, 13.5 $C_{14}H_{10}N_2S$ requires C, 70.6; H, 4.2; N, 11.8; S, 13.5%). δ_H 7.43 (4H, d), 7.48 (2H, d), 8.64 (4H, dd); δ_C 119.6 (d), 126.4 (d), 140.5 (s), 142.4 (s), 150.4 (d); were obtained from 2,5-di(2-pyridyl-, 3-pyridyl- and 4-pyridyl)butan-1,4-dione, respectively.

General procedures for the N-methylation of monopyridyl systems and N,N-dimethylation of the dipyridyl systems.

Method A: Iodomethane (4.56 g, 32 mmol) and the appropriate monopyridyl system (3 mmol), or the 2,5-di(pyridyl)thiophene or furan (1 mmol), in ethanol (5 ml) were heated under reflux for 5h. The reaction mixture was cooled to room temperature and diethyl ether (2 ml) was added to cause the precipitation of the quaternised salt, which was recrystallised from ethanol:diethyl ether.

Method B: The reaction time used in Method A was extended to 10h.

Method C: The reaction time used in Method A was extended to 50h.

Method D: The pyridyl system (1 mmol) and iodomethane (11.4 g, 8 mmol) were heated in a sealed tube at 100°C for 50h. The mixture was cooled for 24 h, and the precipitated salt was collected, washed sequentially with cold ethanol (5 ml) and dichloromethane (10 ml).

Method E: The reaction time used in Method A was extended to 2 weeks.

Using Method A, the furylpyridines **2**, **6** and **10** respectively gave *1-methyl-2-(5-methyl-2-furyl)pyridinium iodide* (76%), m.p. 159.5 - 160°C (Found: C, 43.9; H, 3.9; N, 4.6; I, 42.0 $C_{11}H_{12}NOI$ requires C, 43.9; H, 4.0; N, 4.7, I, 42.1%). δ_H 2.46 (3H, s), 4.64 (3H, s), 6.26 (1H, d), 7.64 (1H, d), 7.93 (1H, dd), 8.20 - 8.70 (2H, m), 9.35 (1H, dd); δ_C 14.5 (q), 49.6 (q), 111.3 (d), 123.4 (d), 124.7 (d), 126.1 (d), 141.1 (d), 141.4 (s), 144.9 (s), 146.6 (d), 159.6 (s); *1-methyl-3-(5-methyl-2-furyl)pyridinium iodide* (97%), m.p. 180 - 181°C (Found: C, 43.7; H, 3.9; N, 4.5; I, 41.9 $C_{11}H_{12}NOI$ requires C, 43.9; H, 4.0; N, 4.7; I, 42.1%). δ_H 2.38 (3H, s), 4.68 (3H, s), 6.14 (1H, dd), 7.34 (1H, d), 8.02 (1H, m), 8.52 (1H, m), 9.00 (1H, dd), 9.56 (1H, d); δ_C (DMSO-d_6) 13.5 (q), 48.2 (q), 109.3 (d), 112.9 (d), 127.7 (d), 129.4 (s), 136.8 (d), 139.5 (s), 142.2 (s), 144.8 (d), 155.8 (d); *1-methyl-4-(5-methyl-2-furyl)pyridinium iodide* (97%), m.p. 209 - 211°C (Found: C, 43.9; H, 3.9; N, 4.6; I, 42.1 $C_{11}H_{12}NOI$ requires C, 43.9; H, 4.0; N, 4.7; I, 42.1%). δ_H (DMSO-d_6) 2.48 (3H, s), 4.28 (3H, s), 6.54 (1H, dd), 7.76 (1H, d), 8.18 (2H, dd), 8.88 (2H, dd); δ_C (DMSO-d_6) 13.7 (q), 46.7 (q), 110.8 (d) 118.7 (d), 118.9 (d), 142.0 (s), 145.1 (s), 146.3 (s), 158.7 (d).

2,5-Di(2-pyridyl)furan **3** gave *1-methyl-2-(5-(2-pyridyl)-2-furyl)pyridinium iodide* (Method C 45%; Method D 92%), m.p. 201 - 202°C (Found: C, 49.2; H, 3.6; N, 7.5; I, 35.0 $C_{15}H_{13}N_2OI$ requires C, 49.5; H, 3.6; N, 7.7; I, 34.8%). δ_H 4.55 (3H, s), 7.52 (2H, d), 7.98-8.50 (4H, m), 8.66 (3H, d), 9.10 (1H, dd); δ_C 48.3 (q), 111.8 (d), 120.0 (d), 122.2 (d), 124.1 (d), 125.1 (d), 126.2 (d), 137.4 (d), 143.1 (d), 143.6 (s), 144.4 (s), 146.6 (d), 146.8 (d), 149.9 (s), 156.9 (s).

Using Method E, **3** gave a mixture of the mono- and di-methylated products, which were separated by their different solubilities in ethanol using a Soxhlet apparatus over a period of 2 days. The initial fractions gave the mono-methylated product (37%), m.p. 200 - 202°C. Subsequent fractions gave *2,5-di(2-pyridyl)furan bismethiodide* (61%), m.p. 244 - 247°C (Found: C, 38.0; H, 3.0; N, 5.4; I, 50.1 $C_{16}H_{16}N_2OI_2$ requires C, 38.0; H, 3.2; N, 5.5; I, 50.1%). δ_H (DMSO-d_6) 4.48 (6H, s), 8.00 - 8.24 (4H, m), 8.60 - 8.90 (4H, m), 9.16 (2H, dd); δ_C (DMSO-d_6) 48.5 (q), 121.1 (d), 126.7 (d), 127.6 (d), 142.3 (d), 145.0 (s), 146.6 (d), 147.5 (s).

2,5-Di(3-pyridyl)furan bismethiodide (97%), m.p. > 315°C (Found: C, 38.0; H, 3.1; N, 5.4; I, 50.1 $C_{16}H_{16}N_2OI_2$ requires C, 38.0; H, 3.2; N, 5.5; I, 50.1%) was obtained from **7** by Method A. δ_H (DMSO-d_6) 4.43 (6H, s), 7.70 (2H, s), 8.27 (2H, dd), 8.97 (2H, d), 9.09 (2H, d), 9.70 (2H, s); δ_C (DMSO-d_6) 48.2 (q), 113.9 (d), 127.8 (d), 128.6 (s), 138.4 (d), 141.0 (s), 144.0 (d), 148.6 (d).

2,5-Di(4-pyridyl)furan bismethiodide (91%), m.p. 299 - 300°C (Found: C, 37.8; H, 3.2; N, 5.3; I, 50.2 $C_{16}H_{16}N_2OI_2$ requires C, 38.0; H, 3.2; N, 5.5; I, 50.1%) was obtained from **11** by Method A. δ_H (DMSO-d_6) 4.36 (6H, s), 8.09 (2H, s), 8.70 (4H, d), 9.12 (2H, d); δ_C (DMSO-d_6) 47.3 (q), 119.0 (d), 121.2 (d), 141.3 (s), 145.8 (s), 151.5 (d).

Using Method A, the thienylpyridines **4**, **8** and **12** respectively gave *1-methyl-2-(5-methyl-2-thienyl)-pyridinium iodide* (53%), m.p. 125 - 127°C; (Found: C, 41.4; H, 3.7; N, 4.2; S, 10.2; I, 40.2 $C_{11}H_{12}NSI$ requires C, 41.7; H, 3.8; N, 4.4; S, 10.1; I, 40.0%). δ_H (DMSO-d_6) 2.56 (3H, s), 4.36 (3H, s), 7.04 (1H, dd), 7.33 (m, 1H), 7.63 (1H, d), 7.80 - 8.80 (2H, m), 9.13 (1H, d); δ_C (DMSO-d_6) 15.4 (q), 47.1 (q), 119.4 (d), 124.6 (d), 125.5 (d), 132.5 (d), 138.6 (d), 141.7 (s), 142.6 (s), 147.1 (d) 148.2 (s); *1-methyl-3-(5-methyl-2-thienyl)pyridinium iodide* (80%), m.p. 175 - 177°C (Found: C, 41.9; H, 3.8; N, 4.2; S, 10.1; I, 40.0 $C_{11}H_{12}NSI$ requires C, 41.7; H, 3.8; N, 4.4; S, 10.1; I, 40.0%). δ_H (DMSO-d_6) 2.54 (3H, s), 4.46 (3H, s), 7.01 (1H, dd), 7.78 (1H, d), 8.11 (1H, t,), 8.72 (1H, d), 8.91 (1H, d), 9.37 (1H, s); δ_C (DMSO-d_6) 15.2 (q), 48.1(q), 127.5 (d), 127.6 (d), 128.3 (d), 132.7 (d), 133.3 (d), 139.3 (s), 141.0 (s), 142.5 (d), 143.8 (d); *1-methyl-4-(5-methyl-2-thienyl)pyridinium iodide* (90%), m.p. 163 - 165°C (Found: C, 41.7; H, 4.0; N, 4.3; S, 10.1; I, 39.9 $C_{11}H_{12}NSI$ requires C, 41.7; H, 3.8; N, 4.4; S, 10.1; I, 40.0%). δ_H (DMSO-d_6) 2.58 (3H, s), 4.35 (3H, s), 7.06 (1H, dd), 8.16 (3H, dd), 8.91 (2H, d); δ_C (DMSO-d_6) 15.6 (q), 46.8 (q), 121.0 (d), 128.8 (d), 132.4 (d), 134.2 (s), 145.0 (s), 147.2 (s), 148.8 (d).

Using Method E, 2,5-Di(2-pyridyl)thiophene **5** gave *2,5-di(2-pyridyl)thiophene bismethiodide* (91%), m.p. 256 - 257°C (Found: C, 36.6; H, 3.1; N, 5.2; S, 6.1; I, 48.4 $C_{16}H_{16}N_2SI_2$ requires C, 36.8; H, 3.1; N, 5.4; S, 6.1; I, 48.6%). δ_H (DMSO-d_6) 4.87 (6H, s), 8.43 (2H, s), 8.60 - 8.90 (4H, m), 9.08 - 9.17 (1H, m), 9.75 (1H, dd); δ_C (DMSO-d_6) 47.6 (q), 127.3 (d), 130.6 (d), 133.4 (d), 135.8 (d), 145.3 (s), 147.2 (d), 147.5 (s). (Methods A and B failed to give any N-methylated derivatives).

Using Method A, the 3- and 4-pyridyl isomers **9** and **13** respectively gave *2,5-di(3-pyridyl)thiophene bismethiodide* (96%), m.p. 274 - 276°C (Found: C, 36.5; H, 3.0; N, 5.2; S, 6.1; I, 48.8 $C_{16}H_{16}N_2SI_2$ requires C, 36.8; H, 3.1; N, 5.4; S, 6.1; I, 48.6%). δ_H (DMSO-d_6) 4.43 (6H, s), 8.10 (2H, s), 8.22 (2H, dd), 8.86 (2H, d), 8.96 (2H, d), 9.52 (2H, s); δ_C (DMSO-d_6) 48.2 (q), 127.9 (d), 129.7 (d), 132.3 (s), 138.2 (d), 142.3 (s), 143.9 (d), 147.5 (d) and *2,5-di(4-pyridyl)thiophene bismethiodide* (96%), m.p. 279 - 281°C (Found: C, 36.8; H, 3.1; N, 5.1; S, 6.3; I, 48.4 $C_{16}H_{16}N_2SI_2$ requires C, 36.8; H, 3.1; N, 5.4; S, 6.1; I, 48.6%). δ_H (DMSO-d_6) 4.35 (6H, s), 8.52 (3H, d), 9.06 (4H, d); δ_C (DMSO-d_6) 47.2 (q), 122.6, (d) 133.3 (d), 142.2 (s), 145.8 (s), 146.1 (d).

Attempted Conversion of Pyridylbutan-1,4-dione polymer 17 into Pyridine:furan polymer 18:

The polymeric diketone[1] **17** (0.5 g) was stirred with polyphosphoric acid (10 g) for 12h at 180 - 190°C. The brown oil was poured onto crushed ice (100 g). The insoluble polymeric material was collected and washed sequentially and repeatedly with water, ethyl acetate, dichloromethane and ethanol to give a product (0.31 g) m.p. > 300°C, which could not be purified further. (Found: C, 64.4; H, 2.2; N, 8.2 $(C_9H_5NO)_n$ (**18**) requires C, 75.5; H, 3.5; N, 9.8% ; $(C_9H_7NO_2)_n$ (**17**) requires C, 67.1; H, 4.4; N, 8.7%). $\nu_{max.}$ (KBr) 1580, 1545, 1450 cm^{-1}. δ_C (solid state) 123.2, 136.5, 144.4, 148.1 p.p.m.

Attempted Conversion of Pyridylbutan-1,4-dione polymer 17 into Pyridine:thiophene polymer 19:

The polymeric diketone[1] **17** (0.81 g) and Lawesson's reagent (1.69 g) in 1,2-dichlorobenzene (65 ml) was heated at 190°C under an atmosphere of nitrogen for 50h. The reaction mixture was allowed to cool to room temperature and the insoluble material was collected and washed sequentially and repeatedly with water, ethyl acetate, dichloromethane and ethanol to give a product (0.61 g) m.p. > 300°C, which could not be purified further. (Found: C, 59.7; H, 4.0; N, 5.4; S, 14.8 $(C_9H_5NS)_n$ (**19**) requires C, 67.9 H, 4.0; N, 8.8; S, 20.1%). $\nu_{max.}$ (KBr) 1565 1500, 1445 cm^{-1}. δ_C (solid state) 113.4, 123.1, 131.6, 134.6, 151.0 p.p.m.

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